

# **Rhabdomyolysis**

## **Form Pathogenesis to Bedside**

**Mohammed Abdel Gawad**

Nephrology Specialist  
Kidney & Urology Center (KUC)  
Alexandria - EGY  
[drgawad@gmail.com](mailto:drgawad@gmail.com)

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## CRUSH INJURIES WITH IMPAIRMENT OF RENAL FUNCTION

BY

E. G. L. BYWATERS, M.B., B.S., M.R.C.P.

*Beit Memorial Fellow*

AND

D. BEALL, Ph.D., Toronto

(From the Departments of Medicine and Pathology, British Postgraduate Medical School)

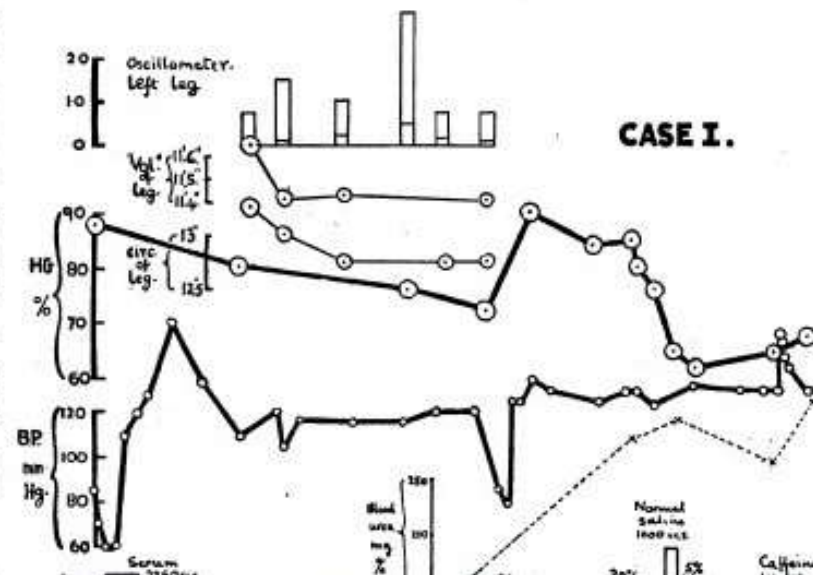
[WITH SPECIAL PLATE]

Amongst air-raid casualties seen at this hospital have been four cases of crush injury of the limbs which, because of the general similarity of their clinical course, were thought to represent a specific and hitherto unreported syndrome, and one which has been and will be seen elsewhere during the war. Such a condition may have been observed in civil practice, but we have been unable to find any account of it in the literature. The cases are of interest on account of the problem propounded by both pathogenesis and treatment. The picture presented by these four cases, and substantiated by others, is briefly as follows:

The patient has

and progress even though the crushed limb be amputated. The urinary output, initially small, owing perhaps to the severity of the shock, diminishes further. The urine contains albumin and many dark brown or black granular casts. These later decrease in number. The patient is

alternately drowsy and anxiously aware of the severity of his illness. Slight generalized oedema, thirst, and incessant vomiting develop, and the blood pressure often remains slightly raised. The blood urea and potassium, raised at an early stage, become progressively higher, and death occurs comparatively suddenly, frequently within a week. Necropsy



During bombing of London in World War II

# Pathogenesis / Causes

**Rhabdomyolysis**

```
graph TD; A[Rhabdomyolysis] --> B[Traumatic]; A --> C[ ]; C --> D[ ];
```

**Traumatic**

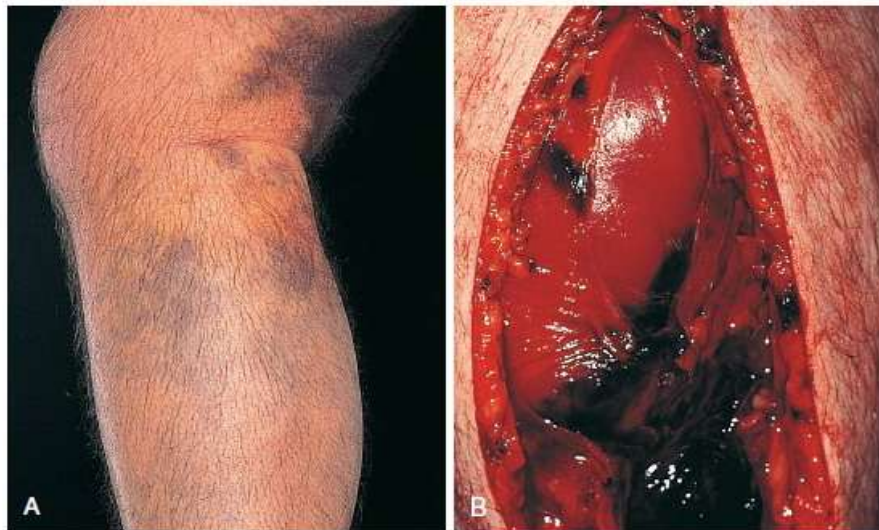
# Traumatic - Rhabdomyolysis

Serum

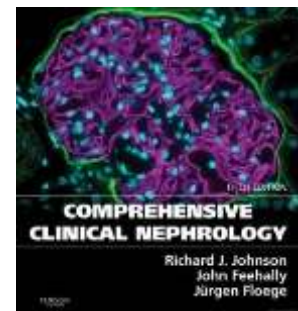
Na  
Ca

CK, LDH  
Purines

Trauma



**Figure 69-9 Compartment syndrome.** A, Severe calf swelling caused by anterior and posterior compartment syndromes after ischemia and reperfusion. B, Appearance after emergency fasciotomy; note edematous muscle and hematoma. (Courtesy Michael J. Allen, FRCS, Leicester, United Kingdom.)



# Traumatic - Rhabdomyolysis

CK, LDH

Purines → Uric Acid

Electrolytes (esp. K<sup>+</sup> and PO<sub>4</sub>)

Aminotransferase enzymes

 **H<sub>2</sub>O**  Lactate

Hypocalcemia, Hypovolemia

Myoglobin

**Trauma**

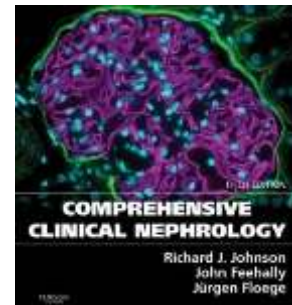
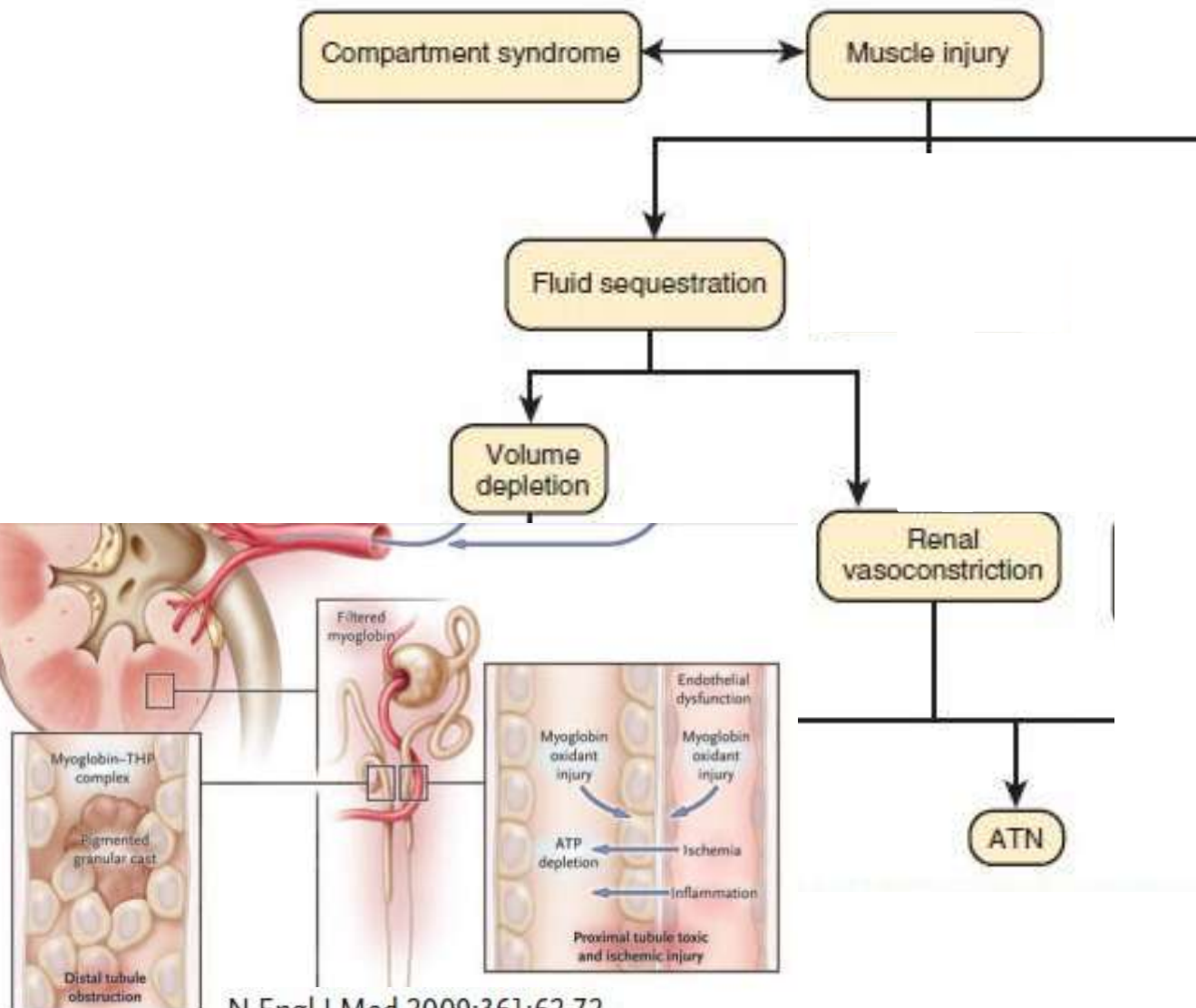
**?? AKI**

Serum

Myocyte Cell

Na  
Ca

# Traumatic - Rhabdomyolysis





# Traumatic - Rhabdomyolysis

CK, LDH

Purines → Uric Acid

Electrolytes (esp. K<sup>+</sup> and PO<sub>4</sub>)

Aminotransferase enzymes

Lactate

Hypocalcemia, Hypovolemia

Myoglobin

ATN

Serum

Myocyte Cell

H<sub>2</sub>O

Na

Ca

# Pathogenesis

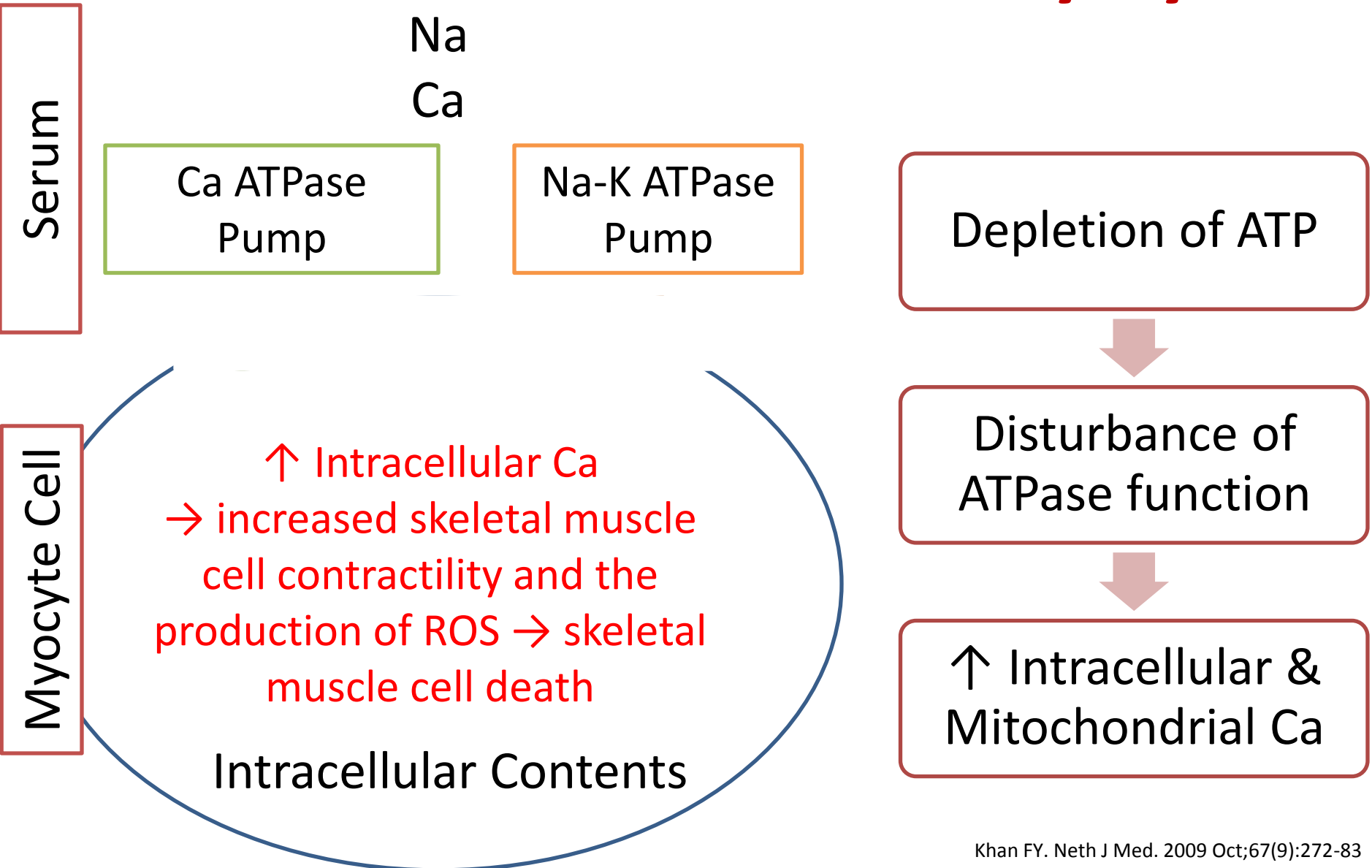
**Rhabdomyolysis**

```
graph TD; A[Rhabdomyolysis] --> B[Non Traumatic];
```

**Non Traumatic**



# Non Traumatic - Rhabdomyolysis

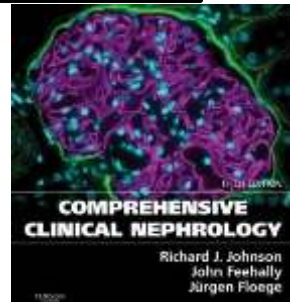


# Pathogenesis - Rhabdomyolysis

## Rhabdomyolysis

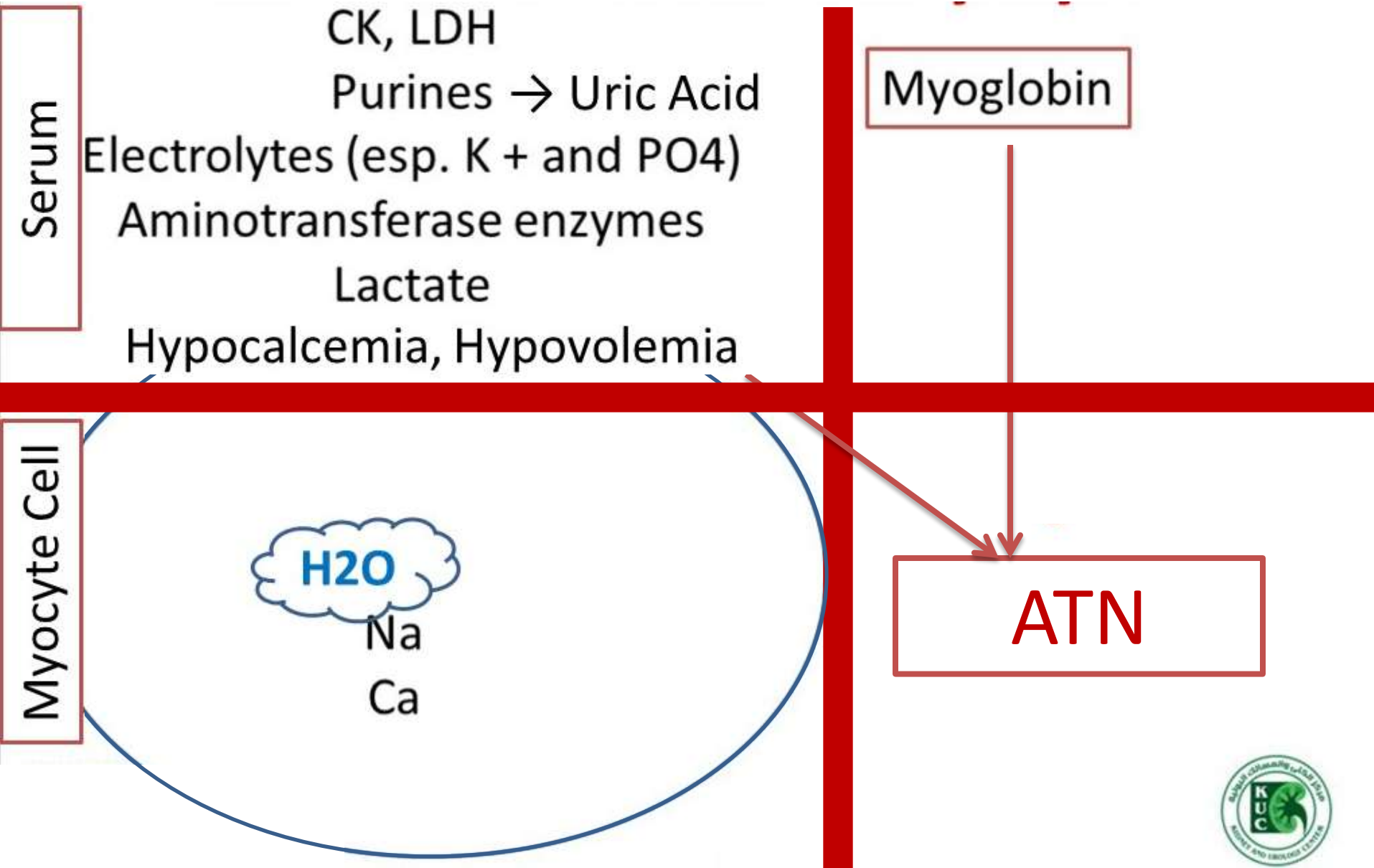
Myofiber exhaustion	Seizures, excessive exercise, heat exhaustion
Toxins	Alcohol, cocaine, heroin, amphetamines, ecstasy, phencyclidine, snakebite
Drugs	Statins, fibrates, zidovudine, neuroleptic malignant syndrome, azathioprine, theophylline, lithium, diuretics
Electrolyte disorders	Hypophosphatemia, hypokalemia, excess water shifts (hyposmolarity)
Infections	Viral (influenza, human immunodeficiency virus [HIV], Coxsackievirus, Epstein-Barr virus), bacterial ( <i>Legionella</i> , <i>Francisella</i> , <i>Streptococcus pneumoniae</i> , <i>Salmonella</i> , <i>Staphylococcus aureus</i> )
Familial	McArdle disease, carnitine palmitoyl transferase deficiency, malignant hyperthermia
Other	Hypothyroidism, polymyositis, dermatomyositis

## Non Traumatic



# When to Suspect?

## Clinical Presentation & Lab Ix



# When to Suspect?

## Clinical Presentation & Lab Ix

- The reported frequency of AKI ranges from 15 to over 50 percent
- CK < 20,000 U/l → lower risk of AKI
- CK levels 5000 U/l + coexisting conditions (sepsis, intravascular volume contraction, acidosis) → AKI risk increases.

ATN

# When to Suspect?

## Clinical Presentation & Lab Ix

Serum

CK, LDH

Purines → Uric Acid

Electrolytes (esp. K<sup>+</sup> and PO<sub>4</sub>)

Aminotransferase enzymes

Lactate

Hypocalcemia, Hypovolemia

Myoglobin

Myocyte Cell

H<sub>2</sub>O

Na

Ca

ATN

# When to Suspect?

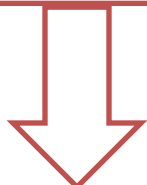
## Clinical Presentation & Lab Ix

### Myoglobin

Myoglobin excreted in urine



Dark, reddish-brown urine  
(+ve dipstick)



-ve microscopic evaluation of  
the urine for RBCs  
*(less than five per high-powered field)*



- Sanders PW, Agarwal A. In: Nabel EG, ed. ACP Medicine, A Textbook of Medicine. Hamilton, Canada: Decker Intellectual Properties; 2010.
- Huerta-Alardín AL. Crit Care. 2005 Apr;9(2):158-69. Epub 2004 Oct 20
- Giannoglou GD. Eur J Intern Med. 2007 Mar;18(2):90-100.



# When to Suspect?

## Clinical Presentation & Lab Ix

### Myoglobin

- Myoglobin appears in the urine when the plasma concentration exceeds 1.5 mg/dL
- Myoglobin has a short half-life of only 2-3 hours
- A suggested role for extrarenal metabolism and clearance of myoglobin

Routine urine testing for myoglobin by urine dipstick evaluation may be negative in up to 50% of patients with rhabdomyolysis

# When to Suspect?

## Clinical Presentation & Lab Ix

Serum

CK, LDH

Purines → Uric Acid

Electrolytes (esp. K<sup>+</sup> and PO<sub>4</sub>)

Aminotransferase enzymes

Lactate

Hypocalcemia, Hypovolemia

Myoglobin

Myocyte Cell

H<sub>2</sub>O

Na

Ca

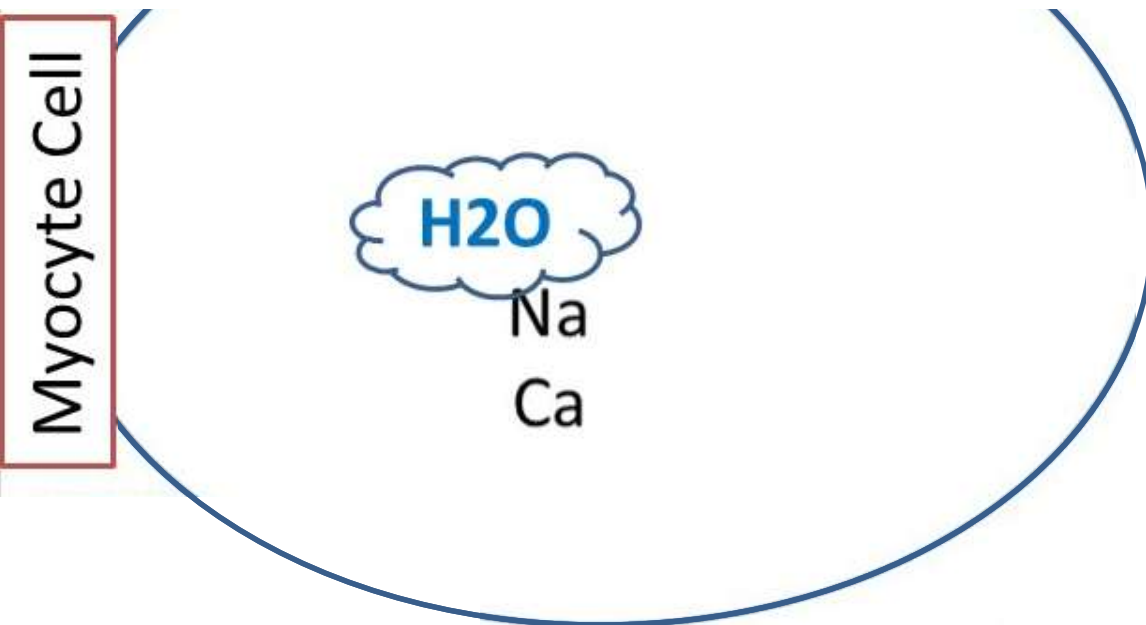
ATN

# When to Suspect?

## Clinical Presentation & Lab Ix

Muscle pain, Weakness

However, more than half of patients may not report muscular symptoms



# When to Suspect?

## Clinical Presentation & Lab Ix

Serum

CK, LDH

Purines → Uric Acid

Electrolytes (esp. K<sup>+</sup> and PO<sub>4</sub>)

Aminotransferase enzymes

Lactate

Hypocalcemia, Hypovolemia

Myoglobin

Myocyte Cell

H<sub>2</sub>O

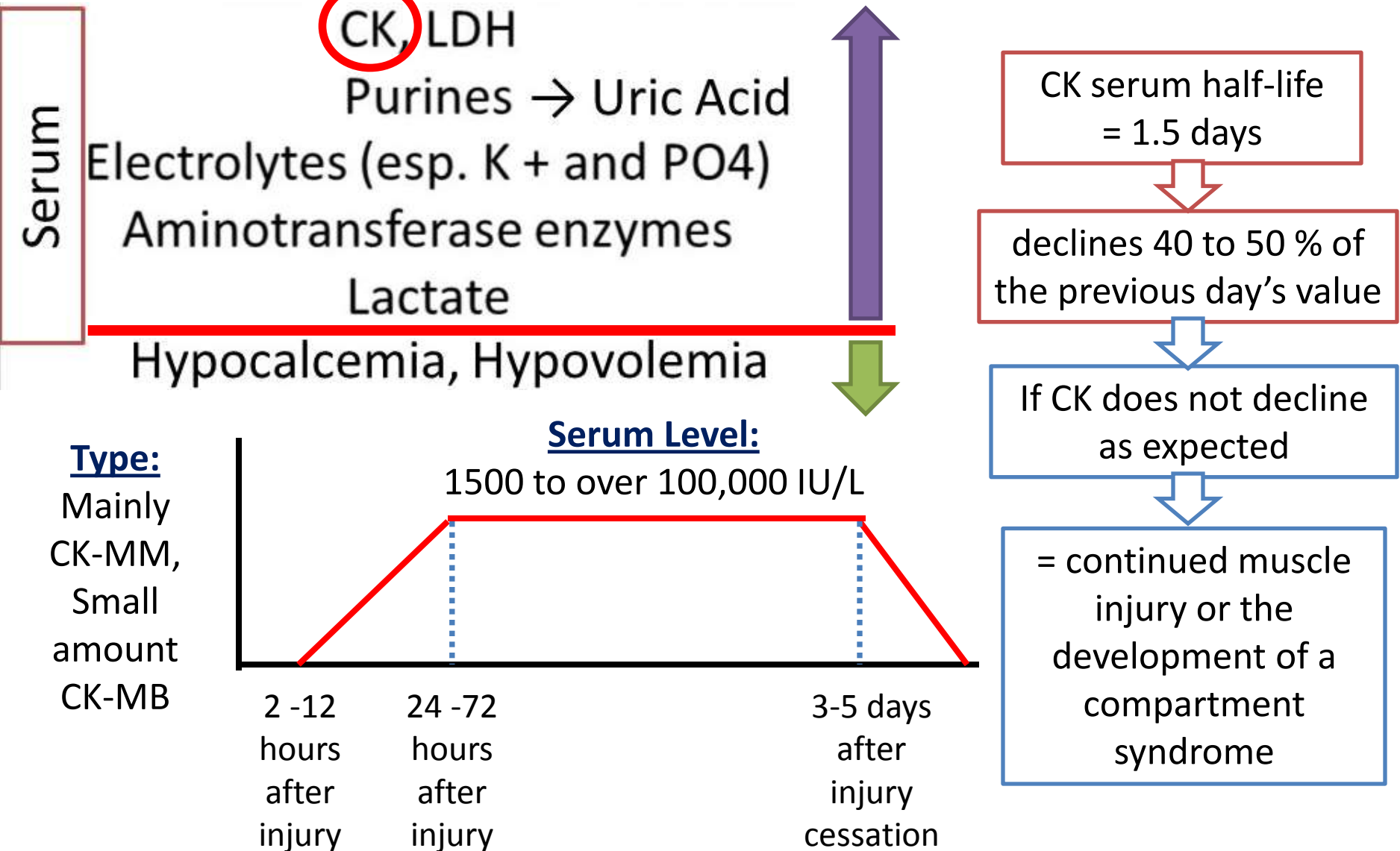
Na

Ca

ATN

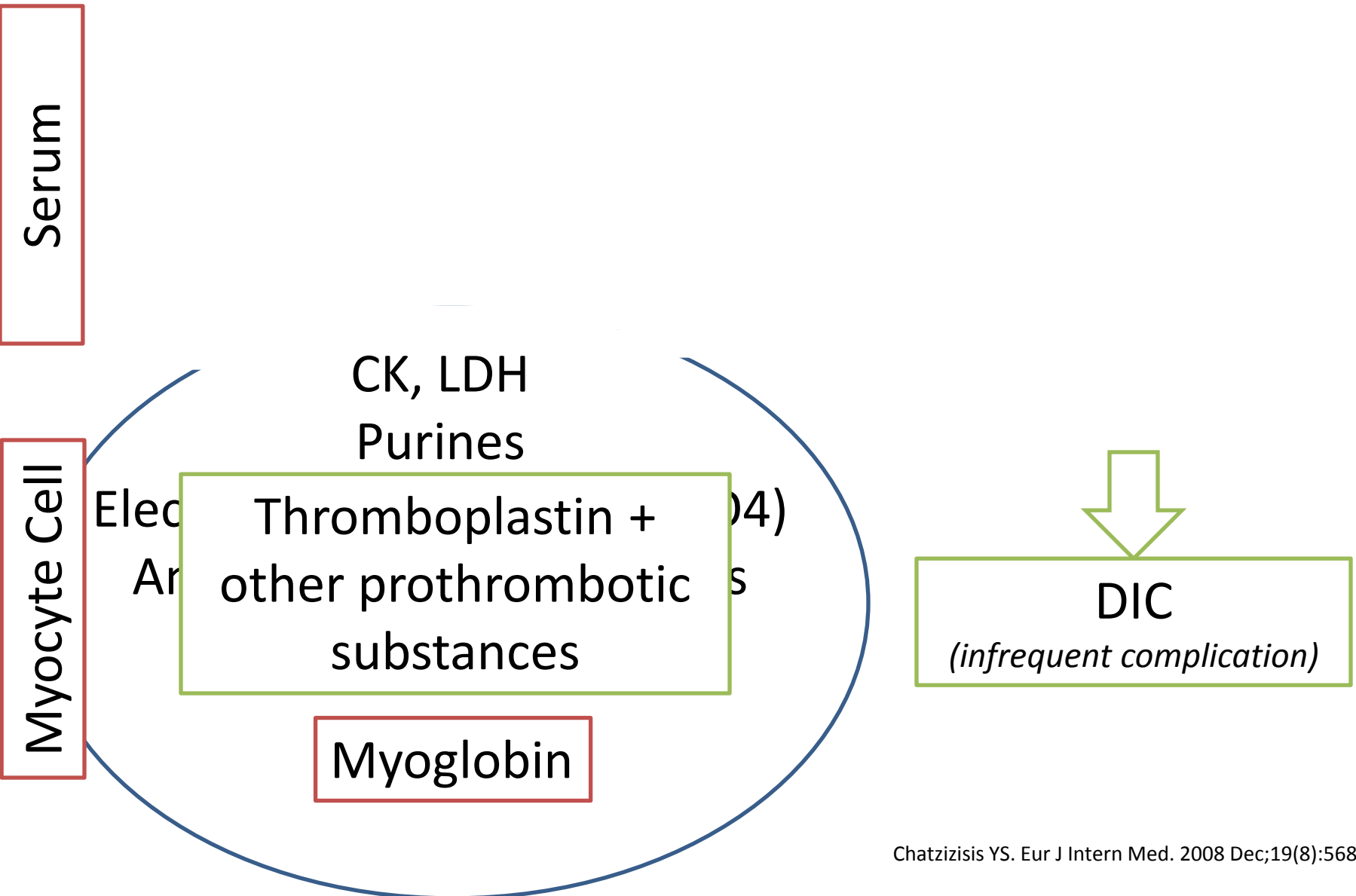
# When to Suspect?

## Clinical Presentation & Lab Ix



# When to Suspect?

## Clinical Presentation & Lab Ix





# Management

1

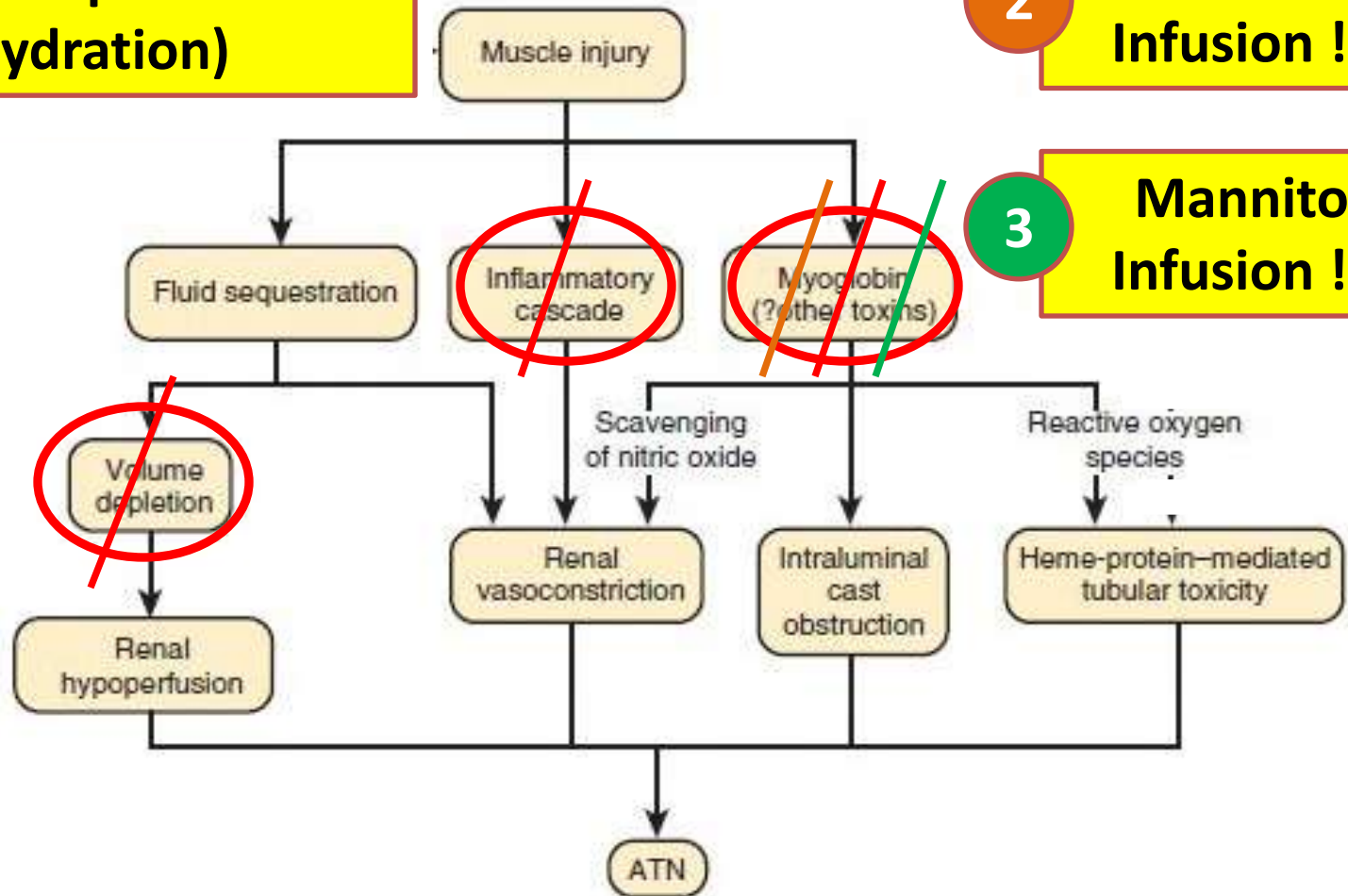
**Volume replacement  
(hydration)**

2

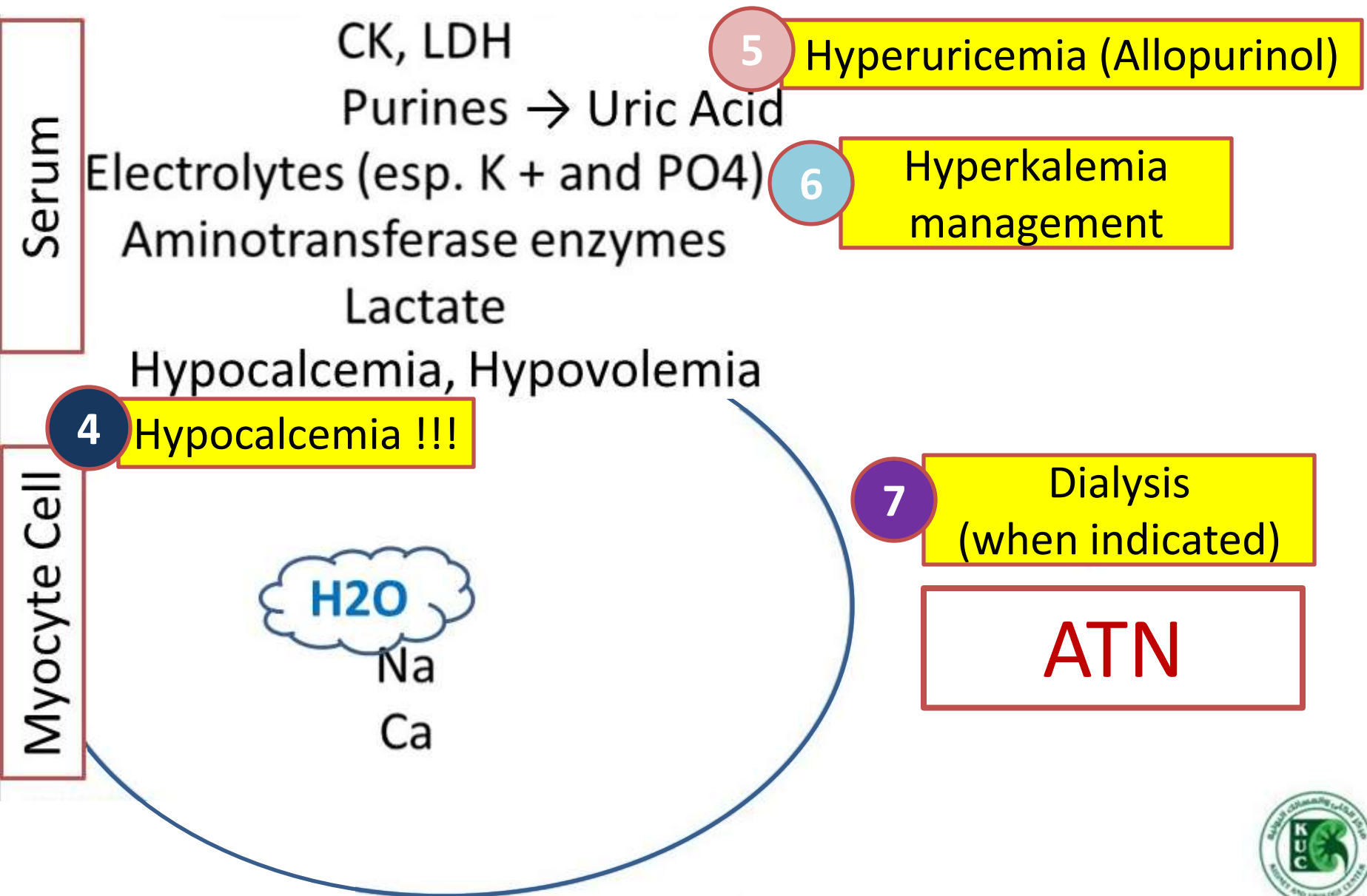
**Bicarbonate  
Infusion !!!**

3

**Mannitol  
Infusion !!!**



# Management



# 1 Volume Replacement (Hydration)

- What? Isotonic saline
- Target? UOP should be maintained around 200-300 ml/h
- Continued until
  - Plasma CK levels decrease to <5000 unit/L
  - Clinical improvement of the cause
  - Urine is dipstick negative for hematuria



# 1 Volume Replacement (Hydration)

## Carefully assess:

Volume status, UOP

(Take care of **HYPERVOLEMIA**)

Compartment syndrome may develop after fluid resuscitation, with worsening edema of the limb and muscle

## 2 Bicarbonate Infusion

To Whom?

When to stop?

Monitor  
art pH &  
Ca / 2hrs

How?

# 3 Mannitol Infusion

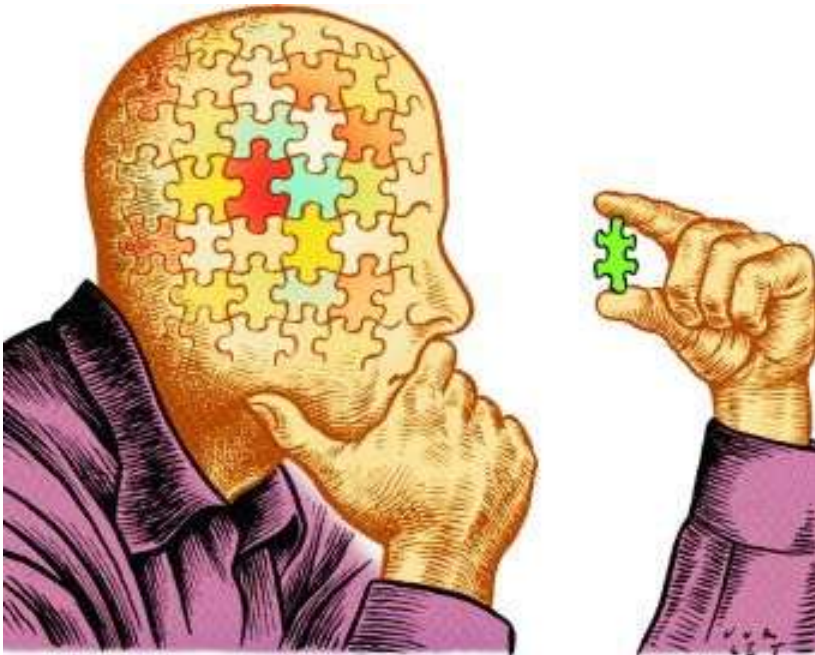
To Whom?

When to stop?

How?



# Evidence !!!



The evidence for the effectiveness of  $\text{NaHCO}_3$  infusion & Mannitol is very weak

## 4 Hypocalcemia

**Give Ca supplement ONLY IF:**

- 1- Symptomatic hypocalcemia
- 2- Management of hyperkalemia

# Treat the cause

- The specific cause is frequently evident from the history or from the immediate circumstances preceding the disorder.
- Consider toxicology screen for drugs, viral screen, TSH if cause not apparent.

# PROGNOSIS

The overall prognosis for patients with heme-induced AKI is favorable as most survivors recover sufficient kidney function to be dialysis independent, and many will recover to normal or near-normal kidney function



- Rhabdomyolysis may be traumatic or non traumatic
- Final common pathway of pathogenesis is the leak of intramuscular contents into circulation
- Final common pathway is sequestration of Ca & H<sub>2</sub>O into muscles
- Hallmark of AKI is ATN



- Dipstick may be –ve for myoglobinuria
- Muscle pain may be absent
- Re-rise of CK = Compartment syndrome or metabolic disorder
- Corner stone of management is hydration





- $\text{NaHCO}_3$  = Precautions = Weak evidence
- Mannitol = Precautions = Weak evidence
- Ca supplement = Precautions
- Prognosis is good

# Thank You

Mohammed Abdel Gawad